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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/812,361	03/30/2004	Giovanni Migliaccio	1570-543	4123

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
AFREMOVA, VERA	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/05/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/812,361	MIGLIACCIO ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-8 are pending and under examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 1-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Sanchez et al. (Amplification of T cells from human cord blood in serum-deprived culture stimulated with stem cell factor, interleukin-7 and interleukin-2". Bone Marrow Transplantation. April 2, 2003. Vol. 31, No. 8, pages 713-723.).

Claims are directed to a method of ex vivo amplification of neonatal T cells comprising the steps of: (a) obtaining light density mononuclear cells from a sample of umbilical cord blood; and (b) stimulating T cell growth by incubating said light density mononuclear cells in a serum deprived culture medium comprising stem cell factor (SCF) and interleukin-7. Some claims are further drawn to use of SCF, IL-7 and IUL-2 combination in the culture medium. Some claim s are further drawn to culturing cells up to 12 days. Some claims are further drawn to the sue of concentration of about 10 ng/ml for each cytokine. Some claims are further drawn to preferential

amplification of CD4+ over CD8+ T cell subsets or to preferential amplification of CD8+ over CD4+ T cell subsets.

The reference by Sanchez et al. discloses an identical method of ex vivo amplification of neonatal T cells derived from mononuclear cells of umbilical cord blood in a serum deprived culture medium comprising stem cell factor (SCF) and interleukin-7 for preferential amplification of CD4+ over CD8+ T cell subsets and further upon addition of IL-2 for preferential amplification of CD8+ over CD4+ T cell subsets (see abstract, for example). Thus, the cited reference anticipates the claimed invention.

2. Claims 1 and 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanchez et al. ("Amplification of the lymphoid compartments in serum-deprived cultures of human cord blood stimulated with SCF, Il-7, IL-4 and IL-2". British Journal of Hematology. 1996. Vol. 93, No. Suppl. 2, pages 293-294.).

Claims are directed to a method of ex vivo amplification of neonatal T cells comprising the steps of: (a) obtaining light density mononuclear cells from a sample of umbilical cord blood; and (b) stimulating T cell growth by incubating said light density mononuclear cells in a serum deprived culture medium comprising stem cell factor (SCF) and interleukin-7. Some claims are further drawn to use of SCF, IL-7 and IUL-2 combination in the culture medium. Some claim s are further drawn to culturing cells up to 12 days. Some claims are further drawn to preferential amplification of CD4+ over CD8+ T cell subsets.

The reference by Sanchez et al. discloses a method of ex vivo amplification of light density mononuclear cells from a sample of umbilical cord blood by stimulating T cell growth in

a serum deprived culture medium with SCF and IL-7 or with SCF, IL-7 and IL-2 from 0 to 10 days. The reference clearly discloses that addition of IL-2 to the combination of SCF and IL-7 results in preferential amplification of CD8+ over CD4+ T cell subsets and, thus, the combination of SCF and IL-7 in the absence of IL-2 results in preferential amplification of CD4+ over CD8+ T cell subsets. The cited reference teaches identical active steps and identical structural elements such as identical starting materials as required by the claimed method and, thus, the disclosed method provides for the same effects as intended for the claimed method. Therefore, the cited reference anticipates the claimed invention.

3. Claims 1-4, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Sanchez et al. (IDS reference; "Thymus-independent T cell differentiation in vitro". Molecular Biology and Hematopoiesis. 1999. 6, pages 51-57.).

The reference by Sanchez et al. discloses a method of ex vivo amplification of light density mononuclear cells from a sample of umbilical cord blood by stimulating T cell growth in a serum deprived culture medium with SCF and IL-7 in concentration 10 ng/ml each (page 52, par. 3) for up to 20 days, thus, including period 0-12 days. The reference teaches that mononuclear cells of umbilical cord blood support differentiation of stem cells into CD4+ or into CD8+ T cell subsets in the serum deprived culture medium with SCF and IL-7 (page 56, last par.). The cited reference teaches identical active steps and identical structural elements such as identical starting materials as required by the claimed method and, thus, the disclosed method provides for the same effects as intended for the claimed method.

Therefore, the cited reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sanchez et al. 1999 (IDS reference; "Thymus-independent T cell differentiation in vitro". Molecular Biology and Hematopoiesis. 1999. 6, pages 51-57) taken with Sanchez et al. 1996 ("Amplification of the lymphoid compartments in serum-deprived cultures of human cord blood stimulated with SCF, Il-7, IL-4 and IL-2". British Journal of Haematology. 1996. Vol. 93, No. Suppl. 2, pages 293-294), Sanchez et al. 2003 (Amplification of T cells from human cord blood in serum-deprived culture stimulated with stem cell factor, interleukin-7 and interleukin-2". Bone Marrow Transplantation. April 2, 2003. Vol. 31, No. 8, pages 713-723) and Skea et al. (IDS reference; "Large ex vivo expansion of human umbilical cord blood CD4+ and CD8+ T cells". Journal of Hematotherapy. 1999. 8, pages 129-139).

Claims are directed to a method of ex vivo amplification of neonatal T cells comprising the steps of: (a) obtaining light density mononuclear cells from a sample of umbilical cord blood; and (b) stimulating T cell growth by incubating said light density mononuclear cells in a serum deprived culture medium comprising stem cell factor (SCF) and interleukin-7. Some claims are further drawn to use of SCF, IL-7 and IUL-2 combination in the culture medium. Some claim s are further drawn to culturing cells up to 12 days. Some claims are further drawn to the sue of concentration of about 10 ng/ml for each cytokine. Some claims are further drawn to preferential

amplification of CD4+ over CD8+ T cell subsets or to preferential amplification of CD8+ over CD4+ T cell subsets.

The cited reference by Sanchez et al. 1999 teaches a method of ex vivo amplification of light density mononuclear cells of umbilical cord blood by stimulating T cell growth in a serum deprived culture medium with SCF and IL-7 in concentration 10 ng/ml each (page 52, par. 3). The reference teaches that mononuclear cells of umbilical cord blood support differentiation of stem cells into CD4+ or into CD8+ T cell subsets in the serum deprived culture medium with SCF and IL-7 (page 56, last par.).

The cited reference by Sanchez et al. 1999 is silent about the use of IL-2. However, the cited reference by Sanchez et al. 1996 and the reference by Sanchez et al. 2003 clearly teach that addition of IL-2 to the combination of SCF and IL-7 results in preferential amplification of CD8+ over CD4+ T cell subsets.

The cited references by Sanchez et al. 1999 and by Sanchez et al. 1996 are silent about concentration of IL-2. However, the reference by Skea et al. demonstrates that in the presence of IL-2 UC blood T lymphocytes are predominantly CD8+ (abstract) and that IL-2 is added in amounts about 10 ng/ml (figures 5 and 6).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to modify the Sanchez et al. 1999 method for ex vivo amplification mononuclear cells of umbilical cord blood by adding IL-2 to the combination of SCF and IL-7 in the serum-deprived medium with a reasonable expectation of success in preferential expansion of CD8+ T cell subsets as adequately demonstrated by the cited prior art references. The particular concentrations of each SSCF, IL-7 and IL-2 as intended for ex vivo

amplification mononuclear cells of umbilical cord blood have been taught and/or suggested by the prior art as adequately demonstrated by the cited references.

Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

August 30, 2006

VERA AFREMOVA

PRIMARY EXAMINER